DuPont Dow Elastomers L. L. C.
Pontchartrain Site
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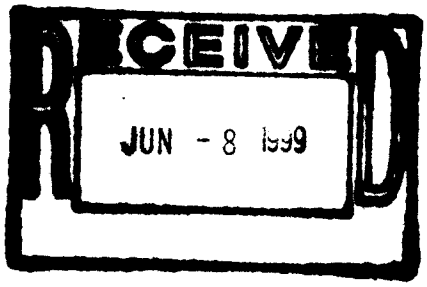
LaPlace, LA 70068-6908
Tel. (504) 536-1141

DuPont Dow elastomers



June 3, 1999

Dr. C. W. Jameson
NIEHS
79 Alexander Drive
Bldg. 4401
Room 3127
Research Triangle Park, NC 27709

Dear Dr. Jameson:

DuPont Dow Elastomers L.L.C. (DuPont Dow) appreciates the opportunity to provide comments on the toxicity and related information for beta-chloroprene (2-chloro-1,3-butadiene or CD) including implications on human carcinogenicity. Our comments address CD production and use, CD Epidemiology, CD Toxicology, an active CD Mechanistic study, human exposure to CD in the US, and IARC Classification of CD. We also separately provide comments on four critical pieces of information that were not previously considered by the NTP Executive Committee (See Appendix 1).

CD Production and Use

Production and use of CD is very limited.

CD is used commercially only as a monomer in polymer manufacture and as an intermediate in the production of 2,3-dichloro-1,3-butadiene, a comonomer subsequently used in polymer manufacture. (A very small amount [<1500 pounds/year] is used in research applications.)

DuPont Dow is one of five worldwide producers of CD, and the only producer and consumer of this material in the United States. All five producers manufacture CD for use in production of polychloroprene, a synthetic elastomer.

Unlike CD, which has a single use, **poly**chloroprene is widely used in a multitude of applications such as adhesives, dipped goods, hoses, power transmission belts, bridge bearing pads, etc. Laymen commonly use the terms chloroprene (CD) and **poly**chloroprene interchangeably. This has led to widespread misconceptions, for example that CD is a component of adhesives or that CD is used in shoe manufacture. However, CD is used only in polymer manufacture.

CD Epidemiology

Epidemiology studies have failed to demonstrate that CD is a human carcinogen.

Two large CD Epidemiology studies conducted in the Soviet Union[1,2] purported to demonstrate an increased risk for lung and skin cancer in CD workers. However, the classification of CD exposure was based on the broadest of employment categories, with no attention to past job history, measured exposure, or comparison to appropriate reference populations. Based on these and other limitations, the Soviet Ministry of Health repudiated the findings from these studies.[3]

Four US studies have been conducted on CD workers at E. I. du Pont de Nemours and Co. (DuPont). These include a cohort mortality study[4] and its subsequent NIOSH-conducted follow-up[5] a cross-sectional study of biochemical and hematologic measurements in CD workers[6] and a case-control study of respiratory cancer deaths at one of the DuPont CD facilities.[7] The first three of these studies showed no significant differences in outcome between the workers exposed to CD and the reference groups. However, the original cohort study was based on active workers and pensioners (effectively, a "survivor" cohort) with 15% lost-to-follow-up. The NIOSH addition reduced the number of individuals lost-to-follow-up to about 1%, but the exposure classifications remained broad and based on job titles rather than actual exposure data. The fourth DuPont study showed an adjusted odds ratio of 4.6 (90% CI = 1.3-16.2) for lung cancer in maintenance workers. This was counterintuitive, however, based on knowledge of job tasks and likely exposures, as the operators, not the maintenance workers should have the highest exposure to CD at DuPont plants. Additionally, of the eight deceased maintenance workers, seven were smokers and no information is available on the smoking history of the eighth. Thus, smoking appeared to be a strong risk factor in these lung cancer deaths.

A retrospective cohort study with a nested case-control study of lung cancer deaths was conducted in China.[8] The study was small with resulting low power, and also had other methodological shortcomings. The exposure characterization was qualitative, and no information was provided on the basis for the classifications. The actual numbers of deaths for both the test and control populations were quite low. Only all cancers combined had at least 5 observed and expected deaths.

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[1] Khachatryan EA. 1972a. The occurrence of lung cancer among people working with chloroprene (Russ.) Vop. Onkol. 18:85-86.
[2] Khachatryan EA. 1972b. The role of choroprene compounds in the process of skin neoplasm formation (Russ.). Gig. Tr. Prof. Zabol., 16:54-55.
[3] Communication (and translation) from Soviet Ministry of Health. (Appendix III)
[4] Pell S. 1978. Mortality of workers exposed to chloroprene. J. Occup. Med. 20:21-29.
[5] Leet TL and Selevan SG. 1982. Mortality analysis of workers exposed to chloroprene. Final report for EI du Pont de Nemours and Co. National Institute for Occupational Safety and Health.
[6] Gooch JJ and Hawn WF. 1981. Biochemical and hematological evaluation of chloroprene workers. J. Occup. Med. 23:268-272.
[7] Chen JL. 1990. Case-control study of respiratory cancer deaths among male employees at Louisville Plant. EI du Pont de Nemours and Co., unpublished report.
[8] Shouqi L, Qinan D, Lyquing L, and Yingfei L. 1989. Epidemiologic study of cancer mortality among chloroprene workers. Biomed. Environ. Sci. 2:141-149.

A cohort mortality study of 660 CD workers was conducted in France, with about 10,000 person-years of follow-up.[9] The results showed no increase in overall mortality with respect to activity sectors or to exposure levels, durations, or periods. Twenty-nine of the 32 total deaths and 58 controls were analyzed in a nested case-control study. No evidence of increased risk was seen for any exposure variable. There was some increased risk for those who had left employment before 1977, but no connection to workplace factors was identified.

While it may be true that negative epidemiological data do not adequately establish the non-carcinogenicity of a suspected material, it does appear that any risk to CD workers must be quite small even under conditions of exposure experienced before the 1970's, which were less stringently controlled and consequently higher than those currently experienced.

A proposed study of CD epidemiology that will address the shortcomings of earlier studies should be completed by 2003. This study, which includes an exposure classification based on measured results, should be of sufficient power to provide valuable information about the human health effects associated with CD exposure. Specifically the University of Cincinnati, under contract to the International Institute of Synthetic Rubber Producers (IISRP), completed a feasibility assessment for an inter-industry study. Based on the findings of the assessment, the IISRP plans to complete a study of 4 international plants, all of which have good quantitative or semi-quantitative exposure data and complete job histories dating from at least 1980. It appears that about 12,000 workers potentially exposed to CD during the last 60 years could be identified.

CD Toxicology

The current chloroprene toxicology data is too inconsistent to justify an RAHC classification for CD.

There are several pieces of information which the NTP reviewers did not consider in determining a recommended carcinogenicity classification for CD. One of the most important of these items is an industry sponsored study conducted at the Dutch Central Institute for Nutrition and Food Research (CIVO). The results of this study are presented in a recent peer-reviewed publication. A copy of the article, H. J Trochimowicz, et al. "Chronic Inhalation Toxicity and Carcinogenic Studies on beta-Chloroprene in Rats and Hamsters", Inhalation Toxicology, 10:443-472,1998 is attached.

[9] Romazini S. Lavdevant G, Lutz JM, Colonna M, and Menegoz F. 1992. Mortality study in occupational exposure to chloroprene. Arch. Mal. Prof. 8:721-725.

There are several important procedural and design differences between the industry sponsored CIVO study and the NTP sponsored toxicology study which was relied upon by RG1 and RG2 and the Board of Scientific Counselors. These include the species, number of animals, exposure concentrations and durations, and CD generation method as tabulated below

Endpoint	CIVO Study	NTP Study
Species/Duration	Syrian hamster/18 months Wistar rat/24 months	B6C3F1 mouse/24 months Fischer 344 rat/24 months
Number of animals	100 per sex/species	50 per sex/species
Exposure concentrations	0, 10 and 50 ppm	0, 12.8, 32 and 80 ppm
Generation conditions	0 deg C vaporization under nitrogen	65 deg C reflux under nitrogen

The CIVO study showed that there was no evidence for the induction of cancer by CD in either rats or hamsters. In addition, no compound-related decreases in survival were found in either rats or hamsters. At 50 ppm, rats showed an increased incidence of alopecia, slight growth retardation and an increased incidence of hepatocellular foci; this latter change was considered a normal response of aging rats. Hamsters showed a slight growth retardation and reduced amyloidosis at 50 ppm but otherwise were not different from controls.

In contrast, the NTP sponsored study reported that CD is a potent multi-site carcinogen in both rats and mice at levels of 12.8 ppm or greater. Also notable are the effects on survival, which was significantly decreased in both rats and mice at 32 ppm in the NTP sponsored study.

While the industry-sponsored study at CIVO used a low temperature vapor generator, the NTP study used a high temperature vapor generation technique which causes thermal reaction of CD to various degradation products. In our limited studies, we have not been able to detect significant differences in the chemical composition of vapor produced using either vapor generation technique. Nonetheless, since we could not reproduce the exact generation and distribution system used by the NTP in their 2-year bioassay, we continue to question whether the differences in results between the two studies can be solely attributed to species/strain differences. The basis for our reservations is as follows:

- Any process that results in chloroprene degradation, such as the heating conditions used in the NTP sponsored bioassay, introduces uncertainties in the experimental results. Heating is counter to standard industry CD safety practices which have been implemented to avoid monomer degradation and violent, exothermic polymerization. CD degradation was reported by Stewart (1971) who demonstrated that CD forms numerous degradation products upon heating. These mixtures of complex degradation products can have toxicological significance as they have been found to be much more potent mutagens than CD alone (Westphal, 1994).

  In the CIVO bioassay, generation conditions were chosen so that CD was never heated, precluding formation of degradation products, whereas CD was continuously heated in the NTP study. While the analytical data from the NTP contract lab indicated that dimers were

not present in the exposure chambers, we believe they used an intrinsically unsound design since any failure of the chilled water cooling system could allow degradation products to be released into the exposure chambers.

- The importance of the generation system becomes apparent when viewed in light of the transgenics studies sponsored by the NTP, who selected the Tg.AC and p53(+/-) transgenics strains specifically for their ability to detect trans-species carcinogens. To this end a 6 month inhalation study was conducted with CD at levels up to 80 ppm using a cold generation technique. Upon study completion, neither the Tg.AC nor p53(+/-) mice developed tumors in any organ. This suggests CD is not a carcinogen in these transgenic strains. The observation that CD did not produce tumors in either of these purportedly sensitive animal models of carcinogenesis using a cold vapor generation method seems contradictory to the relatively potent carcinogenic activity found with CD in the 2 year animal bioassay with the hot vapor generation technique. We believe these differences in tumor outcome raise scientific questions about the validity of the transgenic model to predict carcinogenicity or the veracity of the animal bioassay results from the hot vapor generation technique. In any case, we do not believe that both sets of bioassay data are sufficiently well understood to justify classification of CD as RAHC.

- Confounding the interpretation of the animal bioassay data is the equivocal genetic toxicity data on CD. The in vitro genetic mutation assays show that outcome can vary depending upon the exposure conditions. In standard plate incorporation reverse mutation assays with Salmonella, CD is non-mutagenic. Upon direct gas phase exposure of bacteria, freshly prepared CD also appears non-mutagenic or weakly mutagenic. However, the number of point mutations increases greatly if CD is allowed to age, thereby forming degradation products [Westphal,1994]. The in vivo studies conducted for NTP show that CD is uniformly negative in NTP's battery of genetic toxicity assays for either chromosome damage or repair. This negative finding is particularly significant since the CD used for the in vivo genetic assays was generated by the hot vapor generation method which produces degradation products. Overall, these data suggest that fresh CD has minimal mutagenic activity in point mutation assays; however, activity in these assays can be accentuated if degradation products are present. In contrast, neither fresh nor degraded CD appear to produce chromosome damage. Again, given these uncertainties in the experimental data, we question whether the RAHC classification is appropriate.

  It is our expectation that some of these differences in trans-species responses may be elucidated with appropriate mechanistic and pharmacokinetic studies

CD Mechanistic Study

An in progress study, anticipated to be complete by 2001, will provide a sound scientific basis for assessment of CD human carcinogenicity.

IISRP's Scientific Oversight Committee is conducting a study to elucidate the metabolic fate of CD and determine if differences exist between rodents and humans with regard to the types and amounts of toxic metabolites formed. The project plan involves comparison of in vitro rates of

CD metabolism in liver and lung microsomes across species, assessment of whole animal rates of metabolism, and development of a physiologically-based model that will link the in vitro and whole animal rates of metabolism. Results, to date, show that species dependent metabolic differences exist for CD.

After in vitro incubation of CD with liver microsomes, the disappearance of CD from vial headspace displays saturable Michaelis-Menten kinetic behavior. Estimates of hepatic clearance were 2.5 to 5 times faster for B6C3F1 mice compared with rats, Syrian hamsters, or human liver microsomes. The major metabolite extracted from the liver microsomes was 2-chloro-3,4-epoxy-1-butene. Efforts are underway to synthesize the metabolite for further study, particularly for inter-species comparison of further metabolic activation and/or detoxification. Results from whole animal gas uptake experiments also show that mice metabolize CD more rapidly than do rats. The initial pharmacokinetic model includes chemical specific tissue:air partition coefficients and will be developed to include additional metabolite submodels and their respective in vitro metabolic constants. Because epoxide metabolite(s) of CD may be DNA reactive and thus tumorigenic, studies of metabolism activation and detoxification are key to understanding species/strain dependent carcinogenicity resulting from chronic inhalation studies. This project, which is expected to be complete by 2001 will provide a sound scientific basis for extrapolation of risk from test species to humans.

Human Exposure to CD in the US.

The number of individuals potentially exposed to CD in the US is low.

DuPont Dow is the only domestic producer/consumer of CD. Although millions of pounds/year of CD are produced, less than 200 people are potentially exposed to CD during its manufacture and subsequent conversion to polychloroprene. These individuals are located at the DuPont Dow facilities in Louisville, Ky. and southern Louisiana (Pontchartrain works, near New Orleans). DuPont Dow routinely monitors CD exposure of these potentially exposed individuals using a statistically based program which has been in use for more than 20 years. In addition, DuPont Dow **requires respiratory protection** for any task (even <1 minute duration) where workplace exposure is greater that 1/2 the control limit for that chemical.

CD exposure at DuPont Dow's facilities has decreased significantly since routine employee monitoring was initiated in the 1970's. As an example, twenty years of data for the Louisville Works are shown in Appendix II. As can be seen, the percent of samples containing over 10 ppm CD (internal control limit) and the average concentration show a fairly steady downward trend. The upward spikes in average concentration and "percent over 10 ppm" in 1982, 1986 and 1987/88 reflect that fewer people (jobs) are being monitored, not higher exposure levels. The jobs no longer monitored are those that have been statistically demonstrated to have no potential for exposure above the internal control limit. During the first three years of the program, when essentially all employees were monitored, more than 2000 samples were analyzed each year. As compliance was demonstrated fewer jobs required monitoring so that today less than 100 samples/year are required. Thus, exposure was reduced from an average of 5 ppm for the entire work force (with 14% of the samples >10 ppm) to < 2 ppm for the most highly exposed individuals (with essentially no samples >10 ppm). It is worth noting that, in view of the

mandatory respiratory protection required by DuPont Dow, these personal monitoring results reflect workplace airborne concentrations (i.e. "outside the mask") rather than actual personnel exposure (i.e. "inside the mask").

Recently our internal control limit for CD was lowered from 10 to 2 ppm based, in part, on the data from the NTP sponsored testing. As a result, we are again monitoring significantly larger numbers of jobs, but anticipate that with time workplace exposure levels will be further reduced such that 95% of the samples will again contain less than 1/2 the control level.

Polychloroprene is sold in the form of dry chips and latex (colloidal dispersion of polychloroprene in water). Dry polychloroprene, which represents more than 90% of the total polychloroprene sold, contains no CD (analytical detection limit of 0.5 ppm of CD). Polychloroprene latex contains less than 0.1% chloroprene. As a worst case exposure scenario, DuPont Dow has measured CD concentration inside and outside tanks of polychloroprene latex. Concentrations range from <0.002 ppm outside the tanks to <0.5 ppm 1 foot inside the tank manhole. We conclude from this data, that there is only a de minimus customer exposure hazard from CD.

Computerized mathematical models show that worst case fenceline exposure for our two US. chloroprene handling facilities are <1 ppm during routine operation. Based on historical weather patterns those fenceline exposures are expected to occur <0.1% of the time. Actual community exposures in Houston, Texas during the time a former CD/polychloroprene facility was in operation were significantly less than our predicted fenceline results (normally <5 ppb). We conclude from this data, that there is only a de minimus community exposure hazard from chloroprene.

IARC Classification of CD

IARC says CD is not a probable human carcinogen.

In February 1998, IARC (International Agency for Research on Cancer) reviewed CD and classified it as a possible human carcinogen (2B). IARC considered the negative results of the Industry sponsored inhalation bioassays and the mixed, but predominately negative, CD Epidemiology results in deciding that CD was a possible human carcinogen (class 2B), but not a probable human carcinogen (class 2A). It is worth noting that this decision was made without formal consideration of the negative findings from the NTP's transgenic studies, although their existence was acknowledged. Because IARC's 2A classification is generally considered equivalent to NTP's RAHC classification, it appears IARC does not support a RAHC classification.

Summary and Conclusions

In summary, DuPont Dow maintains that the information set forth above show that:

- DuPont Dow is the only US producer/consumer of CD
- The only commercial use of CD is for polymer manufacture

- There is no epidemiological data that indicates CD is a human carcinogen
- Of the two well documented inhalation bioassays, only the NTP sponsored study show carcinogenicity in animals
- The method of test atmosphere generation used for the NTP bioassay was via a technique inconsistent with actual CD use
- Two other bioassays, utilizing safer, representative generation techniques, provided no evidence of carcinogenicity in animals
- While most studies indicate CD is not genotoxic, some mutagenicity data is equivocal
- A mechanistic study to elucidate these conflicting animal results and develop a science based human health risk assessment should be completed in 2001
- An international epidemiology study based on measured CD exposure should be complete in 2003
- Less than 200 people in the US are potentially exposed to CD during manufacture of CD and Polymer
- Exposure to CD for these 200 people is controlled to low levels
- IARC does not concur with the conclusion that CD is a probable human carcinogen

In conclusion, DuPont Dow submits that the current toxicological database does not justify an RAHC classification at this time. Mechanistic (and epidemiological) data to support or disprove human carcinogenicity will be available within five years. In view of the limited number of people potentially exposed (less than 1 in a 1,000,000 for the US) and the low level of potential exposure, there appears to be minimal risk in delaying classification of CD until this additional data is available.

Sincerely,

M. A. Lynch

Michael A. Lynch
Scientist

APPENDIX I

In order to highlight the significance of several pieces of information not previously considered by NTP[1] in its determination of the carcinogenicity of chloroprene (2-chloro-1,3-butadiene or CD), DuPont Dow Elastomers L.L.C. submits the following summary for consideration by the NTP Executive Committee.

In view of this information and the toxicology/epidemiology studies now in progress,[2] it is the position of DuPont Dow that it is currently unwarranted to classify CD as a Reasonably Anticipated Human Carcinogen. (RAHC)

Newly Published Information Relating to CD Toxicology

H. J. Trochimowicz et al., Chronic Inhalation Toxicity and Carcinogenic Studies on *Beta*-Chloroprene in Rats and Hamsters, Inhalation Toxicology, 10:443-472 (1998)

- The Trochimowicz article presents results of a CD inhalation study sponsored by the major CD producers and conducted by the Dutch Central Institute for Nutrition and Food Research (CIVO)
- No evidence of CD-induced cancer in rats or hamsters was found
- Results indicate CD exposure of up to 50 ppm had no effect on survival of rats or hamsters
- In contrast, results of an NTP-sponsored inhalation study, conducted under different vapor generation conditions, indicate CD reduced animal survival and was a multi-site carcinogen in rats and mice.
- The most significant difference between the CIVO and NTP experimental designs was the method of CD generation

  CIVO generated CD by vaporization at 0°C
  The NTP contractor generated CD vapor by refluxing at 65°C

- It is known that when CD is exposed to elevated temperatures degradation products are produced that are more potent mutagens[3]

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[1] Because these items were not publicly available until recently, the NIEHS/NTP Review Committee for the Report on Carcinogens (RG1), the NTP Executive Interagency Working Group of the Report on Carcinogens (RG2) and the Board of Scientific Counselors Subcommittee did not have the opportunity to review them prior to recommending that chloroprene be listed in the 9th Report on Carcinogens.

[2] *See supra* pp. 5 (IISRP SOC mechanistic study); and pp 2 (University of Cincinatti/IISRP study)

[3] Stewart, 1971; Westphal, 1994.

In view of the conflicting CIVO and NTP results, coupled with the Stewart and Westphal findings, it is submitted that the NTP-sponsored studies do not provide an unequivocal basis upon which classification of CD as a RAHC can be based.

Negative Results of NTP-Sponsored Transgenic Mouse Studies

- An NTP-sponsored 6 month CD inhalation study was conducted using Tg.AC and p53(+/-) transgenic mouse strains specifically selected for ability to detect trans-species carcinogenicity
- The CD generation method used was a low temperature technique like the above-described CIVO inhalation study.
- Neither mouse strain developed tumors in any organ

It is submitted that the NTP–sponsored study suggests CD is not carcinogenic in these assays.

International Agency for Research on Cancer (IARC) Classification of CD

- In February, 1998 IARC reviewed the classification status of CD
- IARC was aware of and considered the CIVO study
- IARC also considered the mixed, but predominately negative CD epidemiology studies
- IARC classified CD as a possible human carcinogen (class 2B), rather than a probable human carcinogen (class 2A)

It is submitted that IARC's assessment of CD as a possible human carcinogen, rather than a probable human carcinogen, suggests that recognized experts in the field, familiar with evaluation of carcinogenic potential, would not support an NTP classification of CD as a "Reasonably Anticipated Human Carcinogen".

Human Exposure to CD in the U.S. Not Significant

- RG1, RG2 and The Board of Scientific Counselors relied on erroneous data from the 1983 NOES survey regarding the number of persons potentially exposed to CD in the U.S.
- NOES erroneously counted persons exposed to polychloroprene as well as those exposed to chloroprene (CD) monomer in arriving at its figure of 17,749 persons potentially exposed
- CD manufacture and use is tightly controlled and exposure occurs almost exclusively during commercial manufacture of CD, a subsequent comonomer and polychloroprene
- The number of persons potentially exposed to CD in the U.S. during CD and Polymer manufacture is less than 200.

- The airborne concentration of CD in the two U.S. plants where CD is manufactured or consumed has typically been measured at less than or equal to 2 ppm
- Actual worker exposure is significantly less than 2 ppm because respiratory protection is required for any task where potential exposure to CD vapor could result in a workplace exposure greater than 1 ppm
- Concentration of residual CD monomer in dry polychloroprene, which constitutes more than 90% of the total polychloroprene sold, is not detectable at a detection limit of 0.5 ppm
- Concentration of residual CD monomer in polychloroprene latex is less than 0.1% and concentrations of CD in the airspace in closed tanks of latex is less than 0.5 ppm

In view of the small number of persons potentially exposed to CD, the low concentration of CD present in exposure settings and the degree of protection required of workers potentially exposed to CD during CD and polymer manufacturing processes, we submit that human exposure to CD in the U.S. is not significant.

It is believed that the above information, not previously considered by NTP, provides compelling evidence that classification of CD by NTP as a "reasonably anticipated human carcinogen" is currently unwarranted. The conflicting data raises questions regarding adequate support for classification of CD as RAHC. In addition, epidemiology and toxicology studies are currently underway that will resolve the conflicting results obtained in earlier studies relied upon by NTP's RG1, RG2 and Board of Scientific Counselors as a basis for CD classification. Moreover, we submit that the number of potentially exposed people in the US doesn't meet the criteria of "a significant number of persons residing in the United States are exposed" cited in Section 301 (b) (4) of the Public Health Service Act. It is therefore respectfully submitted that to include CD in the 9th Report would be an unreasonable and unwarranted burden on U.S. industry.

Louisville Summary Data for personnel exposure to CO (ppm TWA)

YEAR -->	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996
# OF SAMPLES	2331	2691	3676	1739	1520	1288	678	594	674	568	245	73	78	137	9	13	28	15	8	35	14
AVERAGE TWA	5.28	4.84	2.82	2	1.38	0.93	1.07	0.71	1.15	0.77	1.62	2.45	2.51	1.87	0.333	1.08	2.076	1.26	6.2	1.38	0.16
% > 5 ppm	---	---	14.64	6	5	2.41	2.95	1.18	2.79	2.46	2.86	15.07	11.54	10.22	0	0	25	13.3	62.5	5.7	0
% > 10 ppm	13.94	10.22	5.28	3.34	1.05	0.39	2.95	0.34	1.39	0.53	2.04	2.74	5.13	0.73	0	0	0	0	0	2.9	0

Appendix II

APPENDIX III

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ СССР
(Минздрав СССР)

101431, ГСП. Москва К-51.
Рахмановский пер., д. 3.

Телефон 29
Управление внешних сно

29 III.76 № 22/К9-171

на №

г-ну Джону Заппу
Директору "ДюПон де Немур э
Виллингтон, Делавер 19898

копия: Московская контора фирмы
"ДюПон де Немур энд К°"
гост. Метрополь, комн.370
Москва

Уважаемый г-н Запп,

В ответ на Ваше письмо от 6 января с.г. направляем Вам от статьи В.И.Зильфина, Б.С.Фичиджяна и А.М.Погосовой "Результаты изучения хлоропрена на канцерогенность", опубликованную в журнале экспериментальной и клинической медицины АН Армянской ССР (т.XУ, № 3, 1975).

Приложение: упомянутое - 1 экз., только адресату.

С уважением,

М.Н.САВЕЛЬЕВ
Советник - заместитель начальни
Управления внешних сношений

APPENDIX III
TRANSLATION

MINISTRY OF HEALTH USSR

101431 GSP Moscow K-51
Rachmanduskij per., d. 3

Telephone 295-11-40
Administration of Foreign Relations

December 15, 1975 No. 22/89-171

Mr. John Zapp
Director
"Du Pon(t) de Nemour(s) and Co."
Wilmington, Delawar(e) 19898

Copy: Moscow Business Office of
"Du Pont de Nemour(s) and Co."
Hotel Metropol, Room 370
Moscow

Dear Mr. Zapp:

As a supplement to our letter of November 10 of this year we would like to inform you that appropriate competent specialists reviewed the data of research conducted by Dr. E. A. Khachatryan. According to their conclusion, in those investigations some errors in methodology were made, which led to incorrect conclusions.

Papers to that effect will be published shortly in Soviet scientific journals.

With respect,

M. N. Savelev
Councilor - Deputy Chief Administration
of Foreign Relations

Translated by R. Culik, Haskell Laboratory - Edited by Trofimenko.
E. I. du Pont de Nemours and Co.
12-30-75